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| EXAMINER | |
|---|---|
| SISSON, BRADLEY L | |
| ART UNIT | PAPER NUMBER |
| 1634 | |

DATE MAILED: 01/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/756,830 | BRENNER ET AL. | |
| | Examiner | Art Unit | |
| | Bradley L. Sisson | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-4,6,7,15 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112*

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-4, 6, 7, 15, and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claims 1-4, 6, 7, 15 and 16 are indefinite with respect to what constitutes the metes and bounds of both "word" and "minimally cross-hybridizing."

4. For convenience, claims 1 and 15, the only independent claims currently before the Office, are reproduced below.

1. (Currently amended) A method of synthesizing a repertoire of oligonucleotide tags of a predetermined length in the range of from 18 to 60 nucleotides, the method comprising the steps of:

(a) providing a repertoire of same-length oligonucleotide tag precursors in an amplicon, wherein each ~~the~~ oligonucleotide tag precursors ~~each comprising~~ comprises one or more words, and each ~~of the one or more~~ words ~~being~~ is selected from ~~the same~~ a minimally cross-hybridizing set, such that a duplex consisting of a word of the set and the complement of any other word of the set contains a number of mismatches that is either 1, 2 or 3 less than the length of the word;

(b) cleaving the amplicon at a word in each of the oligonucleotide tag precursors to form one or more ligatable ends on each oligonucleotide tag precursor;

(c) ligating one or more words to the one or more ligatable ends to elongate each of the oligonucleotide tag precursors;

(d) amplifying the elongated oligonucleotide tag precursors in the amplicon; and

(e) repeating steps (b) through (d) until a repertoire of oligonucleotide tags having the predetermined length is formed.

15. (Currently amended) A repertoire of cloning vectors for attaching oligonucleotide tags to polynucleotides, wherein each of the vectors comprises a double stranded element corresponding to an oligonucleotide tag of the form:

$$w_1(N)_{x1}w_2(N)_{x2}\ \ldots\ (N)_{xn-1}w_n$$

wherein

each of $w_1$ through $w_n$ is a word consisting of an oligonucleotide having a length from three to fourteen nucleotides or basepairs and being selected from ~~the same~~ a minimally cross hybridizing set, wherein a word of the set and a complement of any other word of the set has a number of mismatches that is either 1, 2 or 3 less than the length of the word ~~at least two mismatches~~;

N is a nucleotide;

each of $x_1$ through $x_{n-1}$ is an integer selected from the group consisting of 0, 1, and 2, provided that at least one of $x_1$ through $x_{n-1}$ is 1 or 2; and

n is an integer in the range of from 4 to 10.

Page 4,last paragraph, provides what could be construed as a definition of the term "word," *infra.*

As used herein, the term "word" means an oligonucleotide selected from a minimally cross-hybridizing set of oligonucleotides, as disclosed in U.S. patent 5,604,097; International patent application PCT/US96/09513; and allowed U.S. patent application Ser. No. 08/659,453; which references are incorporated by reference. An oligonucleotide tag of the invention consists of

5. A review of US Patent 5,604,097 finds but a single incident where the term "word" is used in the same paragraph as that of "minimally cross-hybridizing," and that is found at paragraph 32 of the detailed description, *infra*.

Detailed Description Text - DETX (32):
"The subunits in a minimally cross-hybridizing set code for the monomer added in the library compound. Thus, a nine word set can unambiguously encode library compounds constructed from nine monomers. If some ambiguity is acceptable, then a single subunit may encode more than one monomer. "

The above-reproduced passage has no been found to provide the requisite definition.

6. A search of the text of issued US Patent Application 08/659,453, now US Patent 5,846,719, finds but two instances where the term "word" and "minimally cross-hybridizing" occur in the same paragraph, *infra*.

Detailed Description Text - DETX (22):
When microparticles are used as supports, repertoires of oligonucleotide tags and tag complements may be generated by subunit-wise synthesis via "split and mix" techniques, e.g. as disclosed in Shortle et al, International patent application PCT/US93/03418 or Lyttle et al, Biotechniques, 19: 274-280 (1995). Briefly, the basic unit of the synthesis is a subunit of the oligonucleotide tag. Preferably, phosphoramidite chemistry is used and 3' phosphoramidite oligonucleotides are prepared for each subunit in a minimally cross-hybridizing set, e.g. for the set first listed above, there would be eight 4-mer 3'-phosphoramidites. Synthesis proceeds as disclosed by Shortle et al or in direct analogy with the techniques employed to generate diverse oligonucleotide libraries using nucleosidic monomers, e.g. as disclosed in Telenius et al, Genomics, 13: 718-725 (1992); Welsh et al, Nucleic Acids Research, 19: 5275-5279 (1991); Grothues et al, Nucleic Acids Research, 21: 1321-1322 (1993); Hartley, European patent application 90304496.4; Lam et al, Nature, 354: 82-84 (1991); Zuckerman et al, Int. J. Pept. Protein Research, 40: 498-507 (1992); and the like. Generally, these techniques simply call for the application of mixtures of the activated monomers to the growing oligonucleotide during the coupling steps. Preferably, oligonucleotide tags and tag complements are synthesized on a DNA synthesizer having a number of synthesis chambers which is greater than or equal to the number of different kinds of words used in the construction of the tags. That is, preferably there is a synthesis chamber corresponding to each type of word. In this embodiment, words are

added nucleotide-by-nucleotide, such that if a word consists of five nucleotides there are five monomer couplings in each synthesis chamber. After a word is completely synthesized, the synthesis supports are removed from the chambers, mixed, and redistributed back to the chambers for the next cycle of word addition. This latter embodiment takes advantage of the high coupling yields of monomer addition, e.g. in phosphoramidite chemistries.

Detailed Description Text - DETX (31):
Minimally cross-hybridizing sets of oligonucleotide tags that form triplexes may be generated by the computer program of Appendix Ic, or similar programs. An exemplary set of double stranded 8-mer words are listed below in capital letters with the corresponding complements in small letters. Each such word differs from each of the other words in the set by three base pairs.

The cited passages have not been found to provide a clear meaning to the term. Further, even if one of the cited applications were to have a fixed meaning, the aspect that the instant application stipulates that the term is to be interpreted in light of that presented in several application, application that do not have the same disclosure, further clouds just the true metes and bounds of the term are supposed to be.

7. At page 12 of applicant's representative's response received 01 November 2004, hereinafter the response, said representative directs attention to page 4, lines 28-34, as clearly defining the term. For convenience, the relevant passage has been reproduced below.

> which references are incorporated by reference. An oligonucleotide tag of the invention consists of a plurality of words, or oligonucleotide subunits, that are selected from the same minimally cross-hybridizing set. In such a set, a duplex or triplex consisting of a word of the set and the complement of any other word of the same set contains at least two mismatches. Preferably, a duplex or triplex consisting of a word of the set and the complement of any other word of the same set contains an even larger minimum number of mismatches, e.g. 3, 4, 5, or 6, depending on the length of the words. Still more preferably, the minimum number of mismatches is either 1, 2, or 3 less than the length of the word. Most preferably, the minimum number of mismatches is 1 or 2 less than the length of the word.

The above passage is considered to render the phrase "minimally cross-hybridizing set" ambiguous for while there may be "at least two mismatches" between members of a set, it is unclear if such mismatch needs to be present between all members when, in the formation of a triplex structure, one could seemingly have two fully complementary strands that go to form a duplex structure, and a third strand that would not engage in traditional base pair binding but instead, would bind to the duplex via Hoogstein bonds. In the event that the term is to be applied t the third strand, it is unclear just what constitutes "minimally cross-hybridizing" under such a situation, both with tradition and non-traditional nucleotides being used in one or more of the strands.

8. Said claims are also indefinite where in one instance the claim stipulates that "a duplex consisting of a word," and then there is the "complement of any other word." If a word is "a duplex," it must be comprised of complementary strands. To then state that there is a "complement of any other word" confounds the issue as to what, if anything, the complementary word is in fact complementary to.

9. Claims 2-4, 6, 7, and 16 fail to overcome this issue and are similarly rejected.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-4, 6, 7, and 15-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

12. For purposes of examination, the "repertoire of oligonucleotide tags" to be synthesized by the method of claim 1 can be of virtually any length and nucleotide composition. The claimed method (claims 1-4, 6, and 7) and the claimed product (claims 15 and 16) are considered to be virtually limitless in their scope. The specification fails to provide an adequate written description of such expansive methods and products.

13. The aspect of being able to accurately and reproducibly identify "minimally cross-hybridizing set[s] of oligonucleotides" is critical to the claimed method. As noted above, the cited documents have been improperly incorporated by reference and a such, cannot not be relied upon for satisfaction of written description requirements under 35 USC 112, first paragraph. Furthermore, the specification, even when considering the documents asserted to be incorporated by reference, does not provide an adequate written description of the claimed invention. Page 9, first full paragraph, identifies preferred embodiments and directs the skilled artisan to various

publications. Said publications, and preferred embodiments, including preferred algorithms, have not been incorporated by reference. Accordingly, the specification has not provided an adequate written description of the preferred embodiments of the claimed method. While applicant may assert that certain embodiments of the claimed invention may be obvious to those of skill in the art, obviousness cannot be relied upon for satisfaction of the written description requirement of 35 USC 112, first paragraph. It appears that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

14. While claim 1 is directed to a method of producing a repertoire of oligonucleotide tags, claims 15 and 16 are directed to "a repertoire of cloning vectors." A review of the disclosure fails to find an adequate written description of such a repertoire. At best the disclosure provides suggestions as to how such a repertoire could be produced, but as shown above, such disclosure does not adequately describe how they are to be produced, even when the method is considered in terms of the preferred embodiments.

15. It is well settled that one cannot claim that which they do not yet posses. A review of the disclosure fails to find an adequate written description of the entire genus of vectors so as to reasonably suggest that applicant, at the time of filing, was in possession of same.

16. For the above reasons, and in the absence of convincing evidence to the contrary, claims 1-7 and 15-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

*Response to argument*

17. Applicant's representative, at pages 11, last paragraph, bridging to page 13, asserts that the terms "words," and "minimally cross-hybridizing" are defined by the disclosure, with attention being directed to portions of the disclosure.

18. The above argument ahs been fully considered and has not been found persuasive. As presented above, the terms are deemed not to be defined by the disclosure, whether taken in light of the cite documents or not. While applicant's representative may suggest possible embodiments, such limitations have not been read into the claims.

19. Agreement is reached in that one is not required to teach that which is well known in the art. However, there is no evidence of record that establishes that which is well known in the art. Attention is directed to MPEP 2145.

> Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection. See MPEP § 2129 and § 2144.03 for a discussion of admissions as prior art.
> The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). See MPEP § 716.01(c) for examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration.

20. Claims 1-4, 6, 7, and 15-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth in *Enzo Biochem Inc., v. Calgene, Inc.* (CAFC, 1999) 52 USPQ2d at 1135, bridging to 1136:

> To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).... We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, *e.g.*, *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands*, we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

21. As set forth above, claims 1-4, 6, and 7 are drawn to a method of making oligonucleotide tags, wherein said method fairly encompasses the use of vectors that are also produced by the method. Disclosures critical to enabling the claimed method are not properly incorporated by reference. Indeed, even the preferred embodiments are not found within the four corners of the instant application.

22. The claimed method fairly encompasses producing a repertoire of oligonucleotides that can be of virtually any length. The specification, however, cautions artisans not to produce oligonucleotides above 40-50 nucleotides in length. A review of the specification fails to produce an enabling disclosure whereby skilled artisan are able to overcome the admitted difficulty associated with producing oligonucleotides of such lengths.

23. Assuming *arguendo*, that the claimed oligonucleotides and vectors could be produced, the specification does not enable the use of said oligonucleotides and vectors.

24. The specification provides the following examples:

a. Example 1, "Repertoire Synthesis by Repeated Cycles of Cleavage, Self-Selection, Ligation, and Amplification," pages 14-16;

b. Example 2, "Repertoire Synthesis by Convergent Assembly of Error-free Oligonucleotide Tag Precursors," pages 16-18;

c. Example 3, "Construction of an Eight-Word Tag Library," pages 18-24.

Clearly, the three examples do not each the skilled artisan how to recognize useful over non-useful oligonucleotides or vectors.

2. In view of the breadth of scope clamed, the limited guidance provided, the unpredictable nature of the art to which the claimed invention is directed, and in the absence of convincing evidence to the contrary, the claims are not enabled by the disclosure.

*Response to argument*

25. Argument is advanced at page 13 of the response that the specification, at page 7, second full paragraph, provides an adequate written description of the vectors of claims 15 and 16.

26. For convenience, the cited paragraph is reproduced below.

> The invention further includes repertoires of oligonucleotide tags defined by the following formula:
>
> $$w_1(N)_{x1}w_2(N)_{x2} \ldots (N)_{xn-1}w_n$$
>
> wherein $w_1$, $w_2$, ... $w_n$ are words selected from the same minimally cross-hybridizing set, the words having a length of from three to fourteen nucleotides or basepairs; n is an integer in the range of from 4 to 10; N is a nucleotide or basepair; and $x_1$, $x_2$, ... $x_{n-1}$ are each an integer indicating how many nucleotides or basepairs, N, are present at the given location in the sequence of words, $x_1$, $x_2$, ... $x_{n-1}$ each being selected from the group consisting of 0, 1, 2, 3, and 4, provided that at least one of $x_1$, $x_2$, ... $x_{n-1}$ is 1, 2, 3, or 4. Preferably, $x_1$, $x_2$, ... $x_{n-1}$ are each selected from the group consisting of 0, 1, and 2, provided that at least one of $x_1$, $x_2$, ... $x_{n-1}$ is 1 or 2. Preferably, oligonucleotide tags of the above formula are synthesized by the method of the invention.

As seen above, the paragraph is directed not to the claimed vectors, but to "repertoires of oligonucleotide tags." Accordingly, the argument has not been found persuasive towards the withdrawal of the rejection.

### *Claim Rejections - 35 USC § 102*

27. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

28. Claims 15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Life Technologies (page R-56; 1997).

29. Claims 15 and 16, as amended, have been interpreted a comprising a vector, which is construed as being double stranded, and which comprises at least one "oligonucleotide tag," which in turn has a nucleotide sequence based on the following:

$$w_1(N)_{x1}w_2(N)_{x2} \ldots (N)_{xn-1}w_n$$

wherein

each of $w_1$ through $w_n$ is a word consisting of an oligonucleotide having a length from three to fourteen nucleotides or basepairs and being selected from ~~the same~~ a minimally cross hybridizing set, wherein a word of the set and a complement of any other word of the set has a number of mismatches that is either 1, 2 or 3 less than the length of the word ~~at least two mismatches~~;

N is a nucleotide;

each of $x_1$ through $x_{n-1}$ is an integer selected from the group consisting of 0, 1, and 2, provided that at least one of $x_1$ through $x_{n-1}$ is 1 or 2; and

n is an integer in the range of from 4 to 10.

30. As construed for purposes of examination, there need be at least 4 words ($w_1$, $w_2$, $w_3$, and $w_4$), with each said word being but three nucleotides long. While the formula represents a nucleotide "N" between each word, the intervening nucleotide need not be present as $x_1$ through $x_{n-1}$can be 0, which would leave the formula:

$$w_1w_2w_3w_4$$

and would be but 12 nucleotides in length for claim 15, or 16 nucleotides for claim 16. The limitation of there being a number of mismatches has been construed as encompassing 1, 2, or 3 nucleotides. Accordingly, any three nucleotides that are different by at least one nucleotide from a preceding or succeeding three nucleotides are considered to meet this limitation.

31. Life Technologies teaches the nucleotide sequence of an oligonucleotide and its corresponding nucleotide sequence that is part of a vector (pUC19). As seen therein, there are a vast number of combinations of where the formula $w_1w_2w_3w_4$ can be identified, and which, in accordance with the new limitations, "the number of mismatches ... is either 1, 2 or 3 less than the length of the word."

32. Such a showing is construed to meet the limitations of claims 15 and 16.

***Conclusion***

33. Rejections and/or objections made in the prior Office action and not repeated hereinabove have been withdrawn.

34. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

35. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

36. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

37. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

38. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
23 January 2005